

REMARKS

Applicant thanks Examiner Mi for her time and consideration of the present application during the telephonic interview of February 22, 2011 with the undersigned.

During the interview the present amendment to claim 1 was discussed, as well as the previously provided declarations and cited references. Additionally, it was emphasized that the second vasoactive agent as recited in claim 1 is either (i) *Ginkgo biloba* dimeric flavones, either in a free form or complexed with phospholipids or (ii)amentoflavone.

The application is amended in a manner to place it in condition for allowance.

Status of the Claims

Claims 1 is amended to include the features of claim 2.

Accordingly, claim 2 is cancelled.

Claims 1, 4, 6-10, 13 and 14 are pending.

Claims 6-8 and 10 are withdrawn as being drawn to non-elected groups or species.

Claim Rejections-35 USC §103

Claims 1, 2, 4, 9 and 13 stand rejected under 35 U.S.C. §103(a) as being unpatentable over DI PIERRO WO 02/098436 ("DI PIERRO") in view of BERTINI CURRI et al. US 5,176,919 ("BERTINI

CURRI") and SMITH, III et al. US 2003/0069618 ("SMITH"). This rejection is respectfully traversed for the reasons given below.

The maintained position was that it would have been obvious to use the vasoactive agent visnadine from BERTINI CURRI to treat cellulite in DI PIERRO because BERTINI CURRI teaches visnadine is used for cosmetic treatment of defects caused by insufficient blood perfusion, which includes cellulite, as evidenced by SMITH. The Official Action further maintained that it would have been obvious to exclude the ethyl ximeninate and standardized *Coleus forskolii* extract from DI PIERRO, as they are only optional in DI PIERRO.

However, the proposed combination does not render obvious the claimed invention for at least the two reasons below:

1. The synergistic effect of DI PIERRO was achieved by the combination of five components.

DI PIERRO at page 2, line 15 teaches:

- a) complex of escin/beta-sitosterol with phospholipids,
- b) complex of *Ginkgo biloba* dimeric flavonoids with phospholipids,
- c) complex of *Centella asiatica* triterpenes with phospholipids, and optionally one or both of:
- d) ethyl ximeninate,
- e) standardized *Coleus forskolii* extract.

DI PIERRO shares the same assignee as the present application. During the prosecution of the U.S. counterpart of DI PIERRO (i.e., U.S. Patent No. 7,476,392), a Declaration under Rule 132 was signed by DI PIERRO on July 12, 2007 and filed July 23, 2007. This declaration, which was previously submitted, demonstrated that a synergistic effect is achieved when topically applied from the combination of all five ingredients (a) to (e).

The declaration evaluates the composition of Example 2 (e.g., on page 5 of DI PIERRO), which includes all five components (a) to (e).

Consequently, as evidenced by this declaration, DI PIERRO requires the following components to achieve a synergistic effect:

- a) complex of escin/beta-sitosterol with phospholipids,
- b) complex of *Ginkgo biloba* dimeric flavonoids with phospholipids,
- c) complex of *Centella asiatica* triterpenes with phospholipids,
- d) ethyl ximeninate, and
- e) standardized *Coleus forskolii* extract.

2. The synergistic results are unexpected for the claimed invention.

One would have expected that the synergistic effect taught by DI PIERRO would be achieved by the composition based on the combination of DI PIERRO and BERTINI CURRI with the following active ingredients:

- (a) complex of escin/beta-sitosterol with phospholipids,
- (b) complex of *Ginkgo biloba* dimeric flavonoids with phospholipids,
- (c) complex of *Centella asiatica* triterpenes with phospholipids,
- (d) ethyl ximeninate,
- (e) standardized *Coleus forskolii* extract, and
- (f) visnadine

The claimed composition includes combination of vasoactive agents consisting of:

- (a) a first vasoactive agent
 - i. visnadin or
 - ii. esculoside;
- (b) a second vasoactive agent
 - i. *Ginkgo biloba* dimeric flavones, in a free form or complexed with phospholipids or
 - ii. amentoflavone; and
- (c) a third vasoactive agent selected from the group consisting of:
 - i. escin,
 - ii. escin beta-sitosterol complexed with phospholipids, and
 - iii. *Centella asiatica* extract in a free form or complexed with phospholipids

The Declarations Under Rule 132 by the named inventor of the present application, Dr. Ezio BOMBARDELLI, filed on May 30, 2007 and June 22, 2010, provided experimental evidence of a synergistic, anti-cellulite effect exerted by the claimed active ingredients in a topical application. The most recently filed declaration of June 22, 2010 demonstrated that the observed anti-cellulite effect is "more than additive" for two topically applied compositions:

- the composition of example 5 of the specification with the following active components:
 - (a) visnadin
 - (b) amentoflavone,
 - (c) *Centella asiatica* extract in a free form or complexed with phospholipids,and
- the composition of example 5 with esculoside in place of visnadin.

The independent claims are commensurate in scope with these evaluated compositions, as they include the above mentioned actives, and amended claim 1, in particular, recites a range for the amount of each active component that includes the amounts described in the two compositions of the declarations.

One would not have expected the synergistic effect from the claimed invention based on the cited references because:

- DI PIERRO requires both ethyl ximeninate and standardized *Coleus forskolii* extract to achieve a synergistic effect. Neither is required to achieve the synergistic effect of the present invention.
- DI PIERRO requires both escin/beta-sitosterol with phospholipids and *Centella asiatica* extract,

respectively. The components are alternatives, which are not required in combination in order to achieve the synergistic effect of the present invention.

- SMITH discloses that creams for treatment, or topically applied compositions, have "minimal" results, and for this reason SMITH requires a heat treatment in combination with a composition containing an active ingredient (See, e.g., [0009] in light of [0025]).

Indeed, one would have had no reasonable expectation for success. The claimed invention includes only two of the ingredients from DI PIERRO (e.g., the complex of *Gingko biloba* dimeric flavonoids with phospholipids and the complex of *Centella asiatica* triterpenes with phospholipids), and one would have expected that this would have disrupted the synergism taught by DI PIERRO and rendered the composition unsatisfactory for the intended purpose of DI PIERRO. Moreover, as SMITH asserts that only minimal results can be obtained by topical application, a new combination of active ingredients would not have been expected to be effective in topical treatment.

Therefore, the claimed invention is non-obvious in view of the proposed combination, and withdrawal of the rejection is respectfully requested.

Conclusion

In view of the amendment to the claims, the declarations provided in the appendix and the foregoing remarks, this application is in condition for allowance at the time of the

next Official Action. Allowance and passage to issue on that basis is respectfully requested.

Should there be any matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned at the telephone number listed below.

The Commissioner is hereby authorized in this, concurrent, and future submissions, to charge any deficiency or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

YOUNG & THOMPSON

/Robert A. Madsen/
Robert A. Madsen, Reg. No. 58,543
209 Madison Street, Suite 500
Alexandria, VA 22314
Telephone (703) 521-2297
Telefax (703) 685-0573
(703) 979-4709

RAM/fb